
A specific E3 ligase/deubiquitinase pair modulates TBP protein levels during muscle differentiation.

Journal: Elife

Publication Year: 2015

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PubMed link: 26393420

Funding Grants: Transcriptional regulation of pluripotency in human embryonic stem cells

Public Summary:

TFIID-a complex of TATA-binding protein (TBP) and TBP-associated factors (TAFs)-is a central component of the Pol II promoter recognition apparatus. Recent studies have revealed significant downregulation of TFIID subunits in terminally differentiated myocytes, hepatocytes and adipocytes. Here, we report that TBP protein levels are tightly regulated by the ubiquitin-proteasome system. Using an in vitro ubiquitination assay coupled with biochemical fractionation, we identified Huwe1 as an E3 ligase targeting TBP for K48-linked ubiquitination and proteasome-mediated degradation. Upregulation of Huwe1 expression during myogenesis induces TBP degradation and myotube differentiation. We found that Huwe1 activity on TBP is antagonized by the deubiquitinase USP10, which protects TBP from degradation. Thus, modulating the levels of both Huwe1 and USP10 appears to fine-tune the requisite degradation of TBP during myogenesis. Together, our study unmasks a previously unknown interplay between an E3 ligase and a deubiquitinating enzyme regulating TBP levels during cellular differentiation.

Scientific Abstract:

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